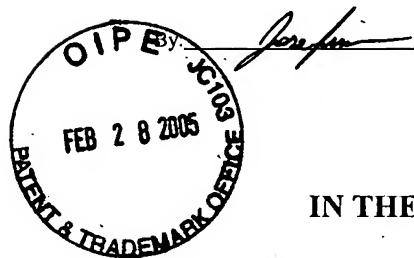


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On 2/25/2005

TOWNSEND and TOWNSEND and CREW LLP



**PATENT**  
Attorney Docket No.: 10692V-000521US  
Client Reference No.: PTQ Ref.: 1997-024-01US

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Michael A. Adams, et al.

Application No.: 10/042,039

Filed: October 25, 2001

For: FORMULATIONS AND  
METHODS OF USING NITRIC OXIDE  
MIMETICS AGAINST A MALIGNANT  
CELL PHENOTYPE

Examiner: To Be Assigned

Art Unit: 1616

**SUPPLEMENTAL INFORMATION  
DISCLOSURE STATEMENT UNDER 37  
CFR §1.97 and §1.98**

Mail Stop Amendment  
Commissioner for Patents  
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Alexandria, VA 22313-1450

Sir:

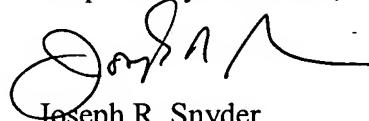
The references cited on the attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 09/842,547, filed April 26, 2001 (Attorney Docket No. 10692V-000520US). It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Also enclosed is a copy of the European Search Report corresponding to the related European Patent Application No. 04105045.1.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

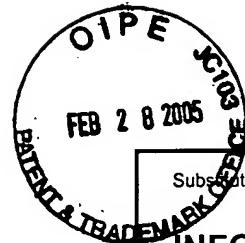
Applicant believes that no fee is required for submission of this statement. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Joseph R. Snyder  
Reg. No. 39,381

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, Eighth Floor  
San Francisco, California 94111-3834  
Tel: 925-472-5000  
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JS:jvl  
60428937 v1



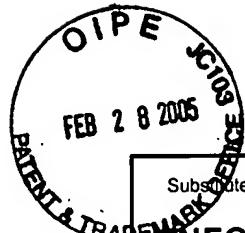
Substitute for form 1449A/PTO				<i>Complete if Known</i>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				Application Number	10/042,039
(use as many sheets as necessary)				Filing Date	October 25, 2001
				First Named Inventor	Adams, Michael A.
				Art Unit	1616
				Examiner Name	To Be Assigned
Sheet	1	of	3	Attorney Docket Number	10692V-000521US

<b>U.S. PATENT DOCUMENTS+</b>					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
1.	5,434,256		07-18-1995	Khokhar et al.	
2.	5,849,790		12-15-1998	Palmer et al.	
3.	6,057,367		05-02-2000	Stamler et al.	
4.	6,103,275		08-15-2000	Seitz et al.	
5.	6,153,186		11-28-2000	Stamler et al.	
6.	6,171,620 B1		01-09-2001	Piver et al.	
7.	6,180,824 B1		01-30-2001	Stamler et al.	
8.	6,203,789 B1		03-20-2001	Stamler et al.	
9.	6,235,782 B1		05-22-2001	Pamukcu et al.	
10.	6,270,779 B1		08-07-2001	Fitzhugh et al.	
11.	2001-0038832 A1		11-08-2001	Bonavida et al.	
12.	2002-0010146 A1		01-24-2002	Garvey et al.	
13.	2003-0092637 A1		05-15-2003	Magnusson et al.	
14.	2003-0215528 A1		11-20-2003	Graham et al.	

<b>FOREIGN PATENT DOCUMENTS</b>						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)		
15.	DE	19732323	C2	08-19-1999	Dunzendorfer	Abstract only <input type="checkbox"/>
16.	WO	96/30336		10-03-1996	Latvian Inst.	<input type="checkbox"/>
17.	WO	98/13358		04-02-1998	Saavedra et al.	<input type="checkbox"/>
18.	WO	99/03462		01-28-1999	Brigham & Young	<input type="checkbox"/>
19.	WO	99/33823		07-08-1999	Towart	<input type="checkbox"/>
20.	WO	99/57306		11-11-1999	Adams et al.	<input type="checkbox"/>
21.	WO	00/51597		09-08-2000	Ouellet et al.	<input type="checkbox"/>
22.	WO	01/54771	A2	08-02-2001	Black et al.	<input type="checkbox"/>
23.	WO	01/70199		09-27-2001	Zhao et al.	<input type="checkbox"/>
						<input type="checkbox"/>

Examiner Signature	Date Considered
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Kind Codes of U.S. Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.



Substitute for form 1449B/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				Application Number	10/042,039
(use as many sheets as necessary)				Filing Date	October 25, 2001
				First Named Inventor	Adams, Michael A.
				Art Unit	1616
				Examiner Name	To Be Assigned
Sheet	2	of	3	Attorney Docket Number	10692V-000521US

<b>NON PATENT LITERATURE DOCUMENTS</b>			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	24.	CARLUCCI et al., "Effect of endothelin-a receptor blockage with atrasentan on tumor progression in men with hormone-refractory prostate cancer: a randomized, phase ii, placebo-controlled trial" J. Clin. Oncol. 21(94):679-689 (2003)	
	25.	CHANG-DUK JUN et al.; "High-dose nitric oxide induces apoptosis in HL-60 human myeloid leukemia cells"; Exper. Molec. Med. 23(2):101-108 (1996)	
	26.	CHEN et al., "Identification of the enzymatic mechanism of nitroglycerin bioactivation" PNAS 99(12):8306-8311 (2002)	
	27.	DOOKERAN, "Mechanisms of antitumor activity for sustained-release nitric-oxide donor, nitroprusside in ethiodol" Proceedings of the Annual Meeting of the American Association for Cancer Research 41(41):280 (2000)	
	28.	ELEY, K. et al., "The effects of pentoxifylline on the survival of human glioma cells with continuous and intermittent stereotactic radiosurgery irradiation" Int. J. Radiat. Oncol. Biol. Phys. 54(2):542-550 (2002)	
	29.	KIM et al., "Type 4 cyclic adenosine monophosphate phosphodiesterase as a therapeutic target in chronic lymphocytic leukemia" Blood 92(7):2484-2494 (1998)	
	30.	MANNICK et al., "Fas-induced caspase denitrosylation" Science 284:651-654 (1999)	
	31.	MARSHALL et al., "Exhaled nitric oxide (NO), NO synthase activity, and regulation of nuclear factor (nf) - kb" Am. J. Respir. Cell Mol. Biol. 21:296-297 (1999)	
	32.	MARSHALL et al., "Nitrosative stress-induced apoptosis through inhibition of nf-kb" J. Biol. Chem. 277(37):34223-34228 (2002)	
	33.	PALLAVICINI, M. et al., "Effect of tumor blood flow manipulations on radiation response" Int. J. Radiat. Oncol. Biol. Phys. 9(9):1321-5 (1983) [Abstract]	
	34.	STIX, G., "Saying yes to NO" Scientific American p. 34 (November, 2001)	
	35.	SUMITANI et al.; "Cytotoxic effect of sodium nitroprusside on cancer cells: involvement of apoptosis and suppression of C-MYC and C-MYB proto-oncogene expression"; Anticancer Res. Hellenic Anticancer Institute 17(2A):865-872 (1997)	
	36.	SUN et al., "Cysteine-3635 is responsible for skeletal muscle ryanodine receptor modulation by NO" PNAS 98(20):11158-11162 (2001)	
	37.	UMANSKY, V. et al., "Activated endothelial cells induce apoptosis in lymphoma cells: role of nitric oxide" Int. J. Oncol. 10:465-471 (1997)	
	38.	UMANSKY, V. et al., "Nitric oxide-mediated apoptosis in human breast cancer cells requires changes in mitochondrial functions and is independent of CD95 (APO-1/Fas)" Int. J. Oncol. 16(1):109-117 (2000)	
	39.	USHMOROV, A. et al., "Nitric oxide-induced apoptosis in human leukemic lines requires mitochondrial lipid degradation and cytochrome C release" Blood 93(7):2342-2352 (1999)	

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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.



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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet	3	of	3	Attorney Docket Number	10692V-000521US
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**Complete if Known**

Application Number	10/042,039
Filing Date	October 25, 2001
First Named Inventor	Adams, Michael A.
Art Unit	1616
Examiner Name	To Be Assigned

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	40.	YP et al., "Topical applications of caffeine or (-)-epigallocatechin gallate (egcg) inhibit carcinogenesis and selectively increase apoptosis in uvb-induced skin tumors in mice" PNAS USA 19:12455-12460 [Abstract]	

Examiner Signature	Date Considered
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

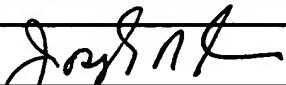
<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

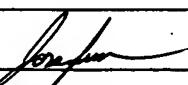
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PTO/SB/21 (09-04)

<b>O I P TRANSMITTAL FORM</b> <b>FEB 28 2005</b> <i>(to be used for all correspondence after initial filing)</i>		Application Number	10/042,039
		Filing Date	October 25, 2001
		First Named Inventor	Michael A. Adams
		Art Unit	1616
		Examiner Name	To Be Assigned
Total Number of Pages in This Submission	10	Attorney Docket Number	10692V-000521US

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to TC
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
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<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Change of Correspondence Address	<input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Copy of European Search Report (4 pages); Return Postcard
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	
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<input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<b>Remarks</b> The Commissioner is authorized to charge any additional fees to Deposit Account 20-1430.	

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT			
Firm Name	Townsend and Townsend and Crew LLP		
Signature			
Printed name	Joseph R. Snyder		
Date	February 25, 2005	Reg. No.	39,381

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Typed or printed name	Jose Luna	Date	February 25, 2005